REMARKS

The present invention provides 3-heterocyclylindazole and -azaindazole compounds of formula I, and the therapeutic use thereof for the treatment of central nervous system disorders related to or affected by the 5-hydroxytryptamine-6 receptor.

Claims 1-20 are pending in this application. Claims 1, 7, 9, 15, 19 and 20 have been amended. Claims 3, 5 and 10-14 have been cancelled.

1. Examiner has required restriction of the claims under 35 USC §121 as follows:

I. Claims 5, 7, 8, 16, 18 and claims 1, 2, 4, 6, 9-15, 19 and 20 in part, drawn to a compound of formula I wherein n is 1; and

II. Claims 1-4, 6, 9-15, 19 and 20 in part, drawn to a compound of formula I wherein n is 2.

Applicants respectfully traverse the foregoing restriction. Applicants point out that all of the compounds of claim 1 contain a common core structure and are the result of the same inventive effort. Thus, Applicants submit that the claims of Groups I and II should be examined together. Notwithstanding the foregoing, and solely in compliance with the provisions of 37 CFR §1.143, Applicants hereby confirm the election with traverse of Group I, Claims 5, 7, 8, 16, 18 and claims 1, 2, 4, 6, 9-15, 19 and 20 in part, drawn to a compound of formula I wherein n is 1. The foregoing amendment reflects this election. Applicants reserve the right to file a divisional application directed to the non-elected subject matter.

2. Claims 9 and 19 have been rejected under 35 USC § 112, second paragraph, as being indefinite. Examiner refers to the second, third and fourth compounds in claims 9 and 19, which lack the term "sulfonyl" and which, therefore, have no antecedent basis in the base claims 1 and 15, respectively.

Claims 9 and 19 have been amended and the second, third and fourth compounds in each claim have been deleted. Applicants believe claims 9 and 19, as amended, meet all of the requirements of 35 USC § 112, second paragraph.

3. Claims 1, 2, 4-8, 10-17 and 20 have been rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for one skilled in the art to make or use the invention. Examiner contends that the exact role of the 5-HT6 receptor has not been established, and that conclusive experimental evidence is lacking for many of the proposed functions of said receptor. Further, Examiner feels that the instant formula I compound does not resemble 5-HT6 antagonists known in the art and indicates that this lack of resemblence implies a lack of selectivity and affinity for the 5-HT6 receptor. Examiner also suggests that the instant data do

not teach whether the formula I compound is an agonist or an antagonist at the 5-HT6 receptor and states that the utility of the formula I compound would be different based on agonist versus antagonist activity. Moreover, Examiner feels that without more teaching and guidance, the breadth of the claims, in combination with the unpredictability of the art, would require undue experimentation.

Applicants respectfully traverse the rejection. While not implying any agreement with Examiner's rejection and solely to advance prosecution, applicants have cancelled method of treatment claims 10-14. Applicants reserve the right to file a continuation application on the subject matter of claims 10-14. Enablement under Section 112, first paragraph, requires that the specification teach those skilled in the art how to make and use the invention without undue experimentation. "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." *MPEP § 2164.01* The role of the 5-HT6 receptor site, and the compounds which bind to said site, in CNS diseases is well established in the art, see attached (A) Behavioural Brain Research, 118 (2001), 107-110; (B) Expert Opinion Therapeutic Patents (2002) 12(4), 513-527; and (C) Current Opinion in Investigational Drugs, (2001) 2(1), 118-122. The modulaton of the 5-HT-6 receptor site is clearly linked to treatment of cognitive dysfunction (A, p. 109; B, p.525 and C, p. 120) and neurodegenerative disease (C, p. 120). The direction of guidance of the specification is toward one of ordinary skill in the art of small molecule pharmaceuticals. The effectiveness of the compounds of the invention is clearly shown in Example 58, Table IV, wherein virtually all of the compounds tested demonstrated 5-HT6 affinity equal to, or greater than, the known pharmaceutical compounds used as test standards. The standards used in Example 58, as well as having a known affinity for the 5-HT6 receptor, have been indicated for use in the treatment of CNS diseases such as Parkinson's disease, schizophrenia, migraine, depression and psychosis. Additionally, the test compounds used in Example 58 demonstrated high selectivity for the 5-HT6 receptor site, increasing the correlation to treatment of CNS disorders affected by the 5-HT6 receptor. It is clear that out of all of the possible compounds in the universe known to be available, or known to be able to be synthesized (truly an infinite number), the select and particular compounds of the present application demonstrate predictable utility in the modulation of the 5-HT6 receptor site and, correspondingly, in the treatment of CNS disorders relating thereto. In support of that correspondence and in support of the level of skill of those in the art, please see attached representative references A, B and C. Considering the serious nature of CNS disorders and the lack of effective treatment therefor, one of ordinary skill in the art would not consider the teachings of the present application to be unpredictable, i.e. to require undue experimentation. In sharp contrast, the skilled artisan would consider the need for experimentation to be greatly diminished by the teachings of the present application. The direction of guidance of the specification is toward one of ordinary skill in the art of small

molecule pharmaceuticals. The chemical and biological examples of the present application clearly teach how to make and use the formula I compound. Applicants submit that there is ample disclosure in the specification to teach one skilled in the art to use the full scope of Applicants' claimed invention. For example, the compounds encompassed by claims 1-9 are all taught in Applicants' application as having affinity for the 5-HT6 receptor site (Detailed Description on page 5, lines 6-13, of the instant specification). Test methods are provided in the application for determining whether a compound has affinity at the 5-HT6 receptor. Applicants also teach that compounds having affinity at the 5-HT6 receptor site have a variety of therapeutic uses as disclosed in the Background section and the Detailed Description section of the application. Thus, applicants have disclosed that all the compounds of the instant invention have affinity at the 5-HT6 site and are thus useful as therapeutic agents to treat a variety of conditions, independent of whether the compound is an agonist or an antagonist. In response to Examiner's statement that "The specification is silent as to whether the inventive compounds are agonists or antagonists.", Section 112, first paragraph, at least with respect to compound or composition claims, does not mandate such a detailed disclosure. "When a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use." *MPEP § 2164.01* Thus, all that is required is that Applicants disclose some use or uses that *in total* covers all the subject matter. Applicants have done this in teaching that the compounds claimed have affinity for the 5-HT6 receptor and disclosing end uses for compounds having affinity for this receptor. The fact that the Examiner finds no evidence in the art that a compound which resembles the formula I compound of the present application acts as a 5-HT6 ligand or is useful for the treatment of CNS disorders is supportive of the patentability of the present application. It is surprising that the formula I compound demonstrates a high affinity for the 5-HT6 receptor. Moreover, enablement for this affinity is clearly supported in the comparative biology Example 58 of the present application wherein all of the formula I compounds tested demonstrated equivalent or superior 5-HT6 binding affinity over that of the known pharmaceutical compounds used as test standards. Accordingly, Applicants respectfully submit that claims 1, 2, 4-8, 15-17and 20 fully meet the requirements of Section 112, first paragraph.

4. Claims 1, 2 and 5 are rejected under 35 USC § 102(b) as being anticipated by Julia (Bull. Soc. Chim. (1964) 8:1939-45). Claims 1, 4, 6 and 15 are rejected under 35 USC § 102(b) as being anticipated by Allen I (US 5861414) and by Vandenberk (US 5196425).

In view of the above amendments, Applicants respectfully traverse the rejection. The claims, as amended hereinabove, are not anticipated by Julia, Allen I or Vandenberk because, as amended, the instant claims do not include formula I compounds wherein Q is CH_2, i.e. 1-

benzylindoles and -indazoles. Applicants believe the rejection under 35 USC § 102(b) has been overcome.

5. Claims 1, 4, 6, 15, 17 and 20 have been rejected under 35 USC § 102(b) as being anticipated by Allen II (WO 97/49698).

In view of the above amendments, Applicants respectfully traverse the rejection. The claims, as amended hereinabove, are not anticipated by Allen II because, as amended, the instant claims exclude those compounds having an acetic acid moiety on the piperidinyl nitrogen, i.e. the definition of R_8 and R_{11} does not include carboxylic acid. Accordingly, Applicants believe the rejection under 35 USC § 102(b) has been overcome.

6. Claims 1, 2, 5, 10-15 and 20 have been rejected under 35 USC § 103(a) as being obvious in view of Hallett (WO 99/47511). Examiner states Hallet's disclosure of a 5-HT2a antagonist 3-piperidinylindole compound, having a hydrogen on the indole nitrogen atom, would motivate one to place an alkyl group on the indolyl nitrogen in order to obtain a 5-HT6 antagonist.

Applicants respectfully traverse the rejection. Without addressing the logic of looking to 5-HT2a antagonists to prepare 5-HT6 ligands, the disclosure of Hallet does not teach or anticipate the compounds of the instant claims. As amended, the instant claims describe formula I compounds having a sulfonyl linkage on the indolyl or indazolyl nitrogen atom. This substitution is distinctly different from the N1 unsubstituted indoles of Hallet. At the time of the invention, one of ordinary skill in the art would not have been motivated to replace the hydrogen of Hallet with the sulfonyl linkage of the instant claims to obtain a 5-HT6 ligand for use in the treatment of a CNS disorder. In view of the foregoing and the amendments set forth hereinabove, Applicants believe the rejection under 35 USC § 103(a) has been overcome.

7. Claims 1, 2 and 4-20 have been rejected under 35 USC § 103(a) as being obvious in view of Strupczewski (US 4670447). Examiner points out that Strupczewski discloses an indazolyl compound and refers to the specific compound of Example 18 in the cited reference.

Applicants respectfully traverse the rejection. The instant claims, as amended, exclude the indazolyl compounds of Strupczewski. There is no teaching or suggestion in Strupczewski to make or use the azaindole, indole or azaindazole compounds of the instant claims. One of ordinary skill would not be motivated by Strupczewski to make the azaindole, indole or azaindazole compounds of the instant invention, since the requisite teaching or suggestion to modify the cited reference is lacking. In view of the foregoing and the amendments set forth hereinabove, Applicants respectfully submit that the rejection under 35 USC § 103(a) has been overcome.

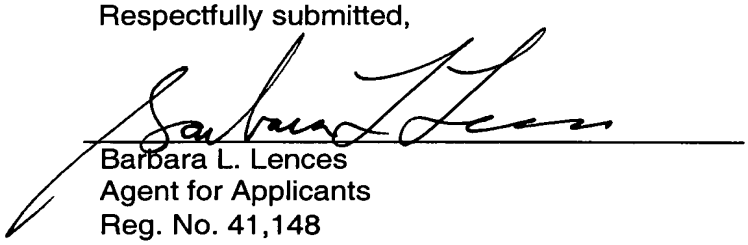
8. Claim 1 has been amended to correct an inadvertant typographical error in the structure. Applicants thank Examiner for pointing out this inadvertant error. Support for this correction can be found in the specification on page 3, lines 5 and 6. Applicants believe no new matter has been introduced by this amendment.

9. In conclusion, Applicants believe that all of Examiner's rejections have been overcome in view of the foregoing and in view of the amendments to the claims, as shown hereinabove. Applicants respectfully request Examiner to enter the above amendments, consider the above remarks, withdraw the rejections and allow the application.

Attached hereto are a page captioned "List of Attached References" and copies of the listed references, which have been discussed hereinabove.

Favorable treatment of the application is earnestly solicited.

Respectfully submitted,



Barbara L. Lences
Agent for Applicants
Reg. No. 41,148

Wyeth
Patent Law Department
Five Giralda Farms
Madison, NJ 07940
Tel. No. (732) 274-4678

LIST OF ATTACHED REFERENCES

A) Meneses, A., Behavioural Brain Research 118 (2001), 107-110

B) Slassi, A., Isaac, M., and O'Brien, A., Expert Opinion Therapeutic Patents (2002) 12(4), 513-527

C) Miguel-Hidalgo, J. J., Current Opinion in Investigational Drugs (2001) 2(1), 118-122